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CONNOLLY BOVE LODGE & HUTZ, LLP
P O BOX 2207
WILMINGTON, DE 19899

EXAMINER	
WORLEY, CATHY KINGDON	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/591,550	SONG ET AL.	
	Examiner	Art Unit	
	CATHY K. WORLEY	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-18 and 20-25* is/are pending in the application.

4a) Of the above claim(s) *4-6,16-18,20 and 21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,7-15 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/30/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed June 30, 2008, has been entered.

2. Claims 2 and 19 have been cancelled.

Claims 1, 3-18, and 20-25 are pending.

Claims 4-6, 16-18, 20, and 21 are withdrawn.

3. Claims 1, 3, 7-15, and 22-25 are examined in the present office action.

4. This application contains claims 4-6, 16-18, 20, and 21 drawn to inventions nonelected with traverse in the response filed Nov. 12, 2007. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

5. The text of those sections of Title 35, U.S. Code not included in this office action can be found in a prior office action.

Objections and Rejections that are Withdrawn

6. The objections to the specification for missing sequence identifiers and for use of trademarks are withdrawn in light of the Applicant's amendments to the specification and sequence listing.

7. The objections to claims 1, 7, and 9 for informalities are withdrawn in light of the Applicant's amendments to the claims.

8. The portion of the rejection under 35 USC 112, 2nd paragraph, for the use of "predominant" and "essentially" and for the recitation of a 100 base pair nucleic acid with 95% identity to SEQ ID NO:1 is withdrawn in light of the Applicant's amendments to the claims.

9. The rejection of claim 7 under 35 USC 112, 2nd paragraph, for missing essential elements is withdrawn in light of Applicant's amendments to the claims.

10. The rejection of claims 1, 3, 7-15, and 22-24 under 35 U.S.C. 102(b) as being anticipated by Donald et al is withdrawn in light of the Applicant's amendments to the claims.

11. The rejection of claims 15 and 24 under 35 U.S.C. 102(b) as being anticipated by Khan A. A. is withdrawn in light of the Applicant's amendments to the claims.

Claim Rejections - 35 USC § 112

12. Claims 1, 3, 7-9, 11-15, and 22-25 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons of record stated in the previous Office Action mailed on Mar. 13, 2008. All dependent claims are included in this rejection; however, the limitations in claims 7 and 10 provide further clarification and therefore claims 7 and 10 are not indefinite and are not included in this rejection. The Applicant's arguments in the response filed on June 30, 2008, were fully considered but were not found to be persuasive.

The term "substantially" in claim 1 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The Applicant argues that the term "substantially" is definite in view of the general guidelines provided in the specification and points to page 23, lines 15-28 as a definition (see second paragraph on page 15 of the response). This is not

persuasive, however, because the specification (on page 23, lines 15-28) does not, in fact, define "substantially", but merely provides several different examples of what "substantially" could mean. This section of the specification, which provides several different possible definitions for "substantially" points out how vague and indefinite this recitation is, because it could be 50% or 80% or 90% of the total biomass of the vegetative organs having expression; or it could mean that there is expression in leafs, stem, and roots, but not in seeds, or it could mean not detectable expression in seed tissue but detectable expression in at least on tissue selected from leafs, stem, and roots. This section of the specification provides at least five different definitions for "substantially", and each of these are different in scope. Therefore, one would not be apprised of the metes and bounds of patent protection covered by the instant recitation which includes "substantially".

Written Description

13. Claims 1, 7-15, and 22-25 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for the reasons of record stated in the previous Office Action mailed on Mar. 13, 2008, and for the reasons stated below. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention. The Applicant's arguments in the response filed on June 30, 2008, were fully considered but were not found to be persuasive.

The claims are broadly drawn to a construct comprising a promoter sequence that is a functional equivalent homolog having at least 98% identity to SEQ ID NO:1 or having a fragment of SEQ ID NO:1 comprising a sequence from about base pair 300 to about base pair 583 of SEQ ID NO:1, and to vectors, organisms, plants, cell-cultures, parts, or propagation materials comprising said construct.

The Applicants describe the promoter of the *Pisum sativum* ptxA gene as SEQ ID NO:1 or its complement (see page 4, lines 42-43). They describe the expression patterns in transgenic Arabidopsis and canola in a Table that indicates high expression in seedlings, medium expression in leaves, roots, flowers and seed pods, and no expression in seeds for Arabidopsis; and high expression in seedlings and leaves, medium expression in flowers, low expression in seed pods, and no expression in seeds for Canola (see Table 1 on page 56). The construct in Example 2 is presumed to comprise SEQ ID NO:1, although this is not expressly stated in the specification. They describe motifs that were identified using computer analysis of the nucleotide sequence of SEQ ID NO:1 (see pages 59-60). They describe a construct comprising a chimeric promoter comprising the ptxa promoter and the maize ubiquitin intron, and they describe the expression pattern from this chimeric promoter as high in embryogenic calli and *in vitro* root, and medium in *in vitro* leaves and plantlets (see Example 17 and Table 3 on page 62).

The essential feature of the promoter recited in the instant claims is that it has promoter activity that is functionally equivalent to SEQ ID NO:1.

They do not describe expression patterns for transformed maize past the T_0 plantlet stage. They do not describe any functional equivalent homologs of SEQ ID NO:1. They do not describe any nucleic acids with 98% identity to SEQ ID NO:1 that retain promoter activity, other than the nucleic acid of SEQ ID NO:1 itself. They do not describe any expression pattern for the promoter of bases 300 to 583 of SEQ ID NO:1.

The recitation of a sequence having at least 98% identity to SEQ ID NO:1 encompasses nucleic acids having additions, deletions, substitutions or insertions relative to SEQ ID NO:1. The Applicants do not describe any additions, deletions, substitutions, or insertions within SEQ ID NO: 1 that retain promoter activity equivalent to the promoter activity of SEQ ID NO:1.

The Federal Circuit has recently clarified the application of the written description requirement to inventions in the field of biotechnology. The court stated that, "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus." See *University of California v. Eli Lilly and Co.*, 119 F. 3d 1559; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

The Applicants fail to describe a representative number of nucleic acid molecules with promoter activity that comprise a nucleotide sequence with additions, deletions, substitutions or insertions into SEQ ID NO:1. The Applicants only describe the nucleic acid of SEQ ID NO:1 which was shown to have promoter activity in transgenic plants. Furthermore, the Applicants fail to describe structural features common to members of the claimed genus of nucleic acids that are sufficient for having promoter activity equivalent to the promoter activity of SEQ ID NO:1. Hence, Applicants fail to meet either prong of the two-prong test set forth by *Eli Lilly*. Furthermore, given the lack of description of the necessary elements essential for promoter activity equivalent to the promoter activity of SEQ ID NO:1, it remains unclear what features identify nucleic acids capable of such activity. Since the genus of nucleic acids has not been described by specific structural features, the specification fails to provide an adequate written description to support the breadth of the claims.

Isolated nucleic acids that have at least 98% identity with SEQ ID NO:1 encompass over 4^{17} nucleotide molecules with additions, deletions, substitutions or insertions into SEQ ID NO:1. This recitation encompasses multitudes of molecules, many of which would not comprise promoter activity equivalent to the activity of SEQ ID NO:1, and most of which were not in the possession of the Applicant at the time of filing. The Applicants have reduced to practice only one promoter (presumed to be SEQ ID NO:1) in an experiment that demonstrates promoter

activity. Accordingly, the specification fails to provide an adequate written description to support the genus of nucleic acids with promoter activity equivalent to SEQ ID NO:1 that comprise a nucleotide sequence with 98% identity to SEQ ID NO:1 as set forth in the claims. (See Written Description guidelines published in 2008 online at http://www.uspto.gov/web/menu/written.pdf).

The Applicant argues that the specification discloses motifs identified within SEQ ID NO:1, and describes, in an indirect manner, the motifs or regions of SEQ ID NO:1 that are unique and most likely related to the promoter function (see first paragraph on page 16 of the response). The Applicant argues that the MsPRP2 promoter has 50% identity and as high as 87% identity of a 100 consecutive base pair sequence to SEQ ID NO:1, but has a different expression pattern compared to SEQ ID NO:1; and the Applicant argues that this guides one of sill in the art because sequences identical between the MsPRP2 promoter and SEQ ID NO:1 are likely not responsible for the specific expression pattern observed (see second paragraph on page 16 of the response). This is not persuasive, however, because it is, yet, another example of the unpredictability of tissue-specificity in promoters. It is highly unpredictable which motifs, domains, or subsequences are responsible for a particular expression pattern, and in the absence of empirically determined expression by deletion analysis or a promoter, it is not possible to predict which bases can be deleted, substituted, or added without altering the tissue-specificity of the promoter.

New Matter

14. Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim has been amended to include the recitation "the same vegetative plant tissue-specific expression" in parts b) and c); ;and this constitutes **NEW MATTER** because the specification does not provide support for this recitation.

Enablement

15. Claims 1, 3, 7-15, and 22-25 remain rejected under 35 U.S.C. 112, first paragraph for the reasons of record stated in the previous Office Action mailed on Mar. 13, 2008, and for the reasons stated below, because the specification, while being enabling for a promoter comprising a fragment of SEQ ID NO:1 wherein said fragment comprises promoter activity in a plant, and wherein the promoter activity is higher in vegetative tissues of Arabidopsis or canola than in seeds of Arabidopsis or canola, and for constructs, vectors, host cells, plants, cell cultures, parts, and propagation material comprising said promoter, does not reasonably provide enablement for a promoter comprising a nucleic acid having 98% identity to SEQ ID NO:1, or for promoter activity in substantially all vegetative tissues of any plants

other than Arabidopsis and canola, and for constructs, vectors, host cells, plants, cell cultures, parts, and propagation material comprising said promoter. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The Applicant's arguments in the response filed on June 30, 2008, were fully considered but were not found to be persuasive.

The claimed invention is not supported by an enabling disclosure taking into account the *Wands* factors. *In re Wands*, 858/F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988). *In re Wands* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and/or use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claim.

The nature of the invention is a molecular biological approach for the heterologous expression of recombinant proteins in transgenic plants.

The claims are broadly drawn to a construct comprising a promoter sequence that is a functional equivalent homolog having at least 98% identity to SEQ ID

NO:1, and to vectors, organisms, plants, cell-cultures, parts, or propagation materials comprising said construct.

The Applicants teach the promoter of the Pisum sativum ptxA gene as SEQ ID NO:1 or its complement (see page 4, lines 42-43). They teach that the expression patterns in transgenic Arabidopsis and canola transformed with a construct comprising the ptxA promoter is high expression in seedlings, medium expression in leaves, roots, flowers and seed pods, and no expression in seeds for Arabidopsis; and high expression in seedlings and leaves, medium expression in flowers, low expression in seed pods, and no expression in seeds for Canola (see Table 1 on page 56). The construct in Example 2 is presumed to comprise SEQ ID NO:1, although this is not expressly stated in the specification. They teach motifs that were identified using computer analysis of the nucleotide sequence of SEQ ID NO:1 (see pages 59-60). They teach a construct comprising a chimeric promoter comprising the ptxA promoter and the maize ubiquitin intron, and they teach that the expression pattern from this chimeric promoter is high in embryogenic calli and *in vitro* root, and medium in *in vitro* leaves and plantlets (see Example 17 and Table 3 on page 62).

They do not teach expression patterns for transformed maize past the T_o plantlet stage. They do not teach any functional equivalent homologs of SEQ ID NO:1. They do not teach any nucleic acids with 98% identity to SEQ ID NO:1 that retain promoter activity, other than the nucleic acid of SEQ ID NO:1 itself. They do

not teach any expression pattern for a construct comprising only the fragment of SEQ ID NO:1 from position 300 to 583 of SEQ ID NO:1 (as claimed in claim 3 and in part b) of amended claim 1). They do not teach expression patterns in any plants other than Arabidopsis, Canola, and T_o maize plantlets.

The recitation of a sequence having at least 98% identity to SEQ ID NO:1 encompasses nucleic acids having additions, deletions, substitutions or insertions relative to SEQ ID NO:1. The Applicants do not teach any additions, deletions, substitutions, or insertions within SEQ ID NO:1 that retain promoter activity equivalent to SEQ ID NO:1.

The state-of-the-art is such that one of skill in the art cannot predict which additions, deletions, substitutions, or insertions within a full-length promoter can be tolerated such that the promoter retains its activity. Mutation of promoter sequences produces unpredictable results. Donald et al (1990, EMBO J. 9:1717-1726) in a mutational analysis of the *Arabidopsis rbcS-1A* promoter found that the effect of a particular mutation was dependent on promoter fragment length (paragraph spanning pg 1723-1724). The region of a given promoter that has a specific activity cannot be predicted and involves the complex interaction of different subdomains (Benfey et al, 1990, Science 250:959-966, see Abstract, Fig. 3-5). Even a very small region may be critical for activity, and the criticality of a particular region must be determined empirically (Kim et al, 1994, Plant Mol. Biol. 24:105-117, Tables 1-4, Abstract, Fig. 1-2).

In addition, the promoter of this invention, the ptxA promoter from *Pisum sativum* (SEQ ID NO:1), was discovered and sequenced by David Phillip Bown, and published in his Ph.D. dissertation in 1992 (see Bown, D. P. Thesis, Dept. of Biol. Sci., Univ. of Durham, Durham, UK (1992)). Bown also deposited the complete genomic sequence, including the promoter, in GenBank Accession X67427 (1997). Bown conducted experiments to determine the expression patterns of the endogenous ptxA gene in *Pisum Sativum*, and he determined that it was expressed strongly in pods, but not in leaves, and only weakly in petals (see second paragraph on page 126; pPP590 is the clone of the ptxA gene). Given this prior art teaching which is in complete opposition to the expression patterns disclosed in Arabidopsis and canola in the instant specification, it is clear that the tissue-specificity of expression from this promoter is different in different plant species. Given this high degree of unpredictability, claims to a particular tissue-specificity are only enabled for the plants in which a tissue specificity has been determined. Note that the experiments in transgenic maize did not proceed past T_o plantlets, therefore, tissue-specificity in stably-transformed maize plants was not determined in the instant application. Note that the fragment recited in claim 3 has not been disclosed to have a particular tissue-specificity in any plant.

In addition, claim 13 recites yeast, algae, and fungi host organisms; and one of skill in the art would not know how to use a yeast, algae or fungi transformed with a construct comprising the ptxA promoter. The ptxA promoter is unlikely to be

active in yeast, algae, or fungi given that it is a plant promoter with tissue-specificity that appears to be dependent on the species of plant in which it is integrated. Therefore, one of skill in the art would not know how to use a yeast, algae, or fungi transformed with a construct comprising an inactive promoter.

Given the lack of guidance in the instant specification, undue trial and error experimentation would be required for one of skill in the art to make multitudes of additions, deletions, substitutions, and insertions and test each one for promoter activity and determine what tissues the promoter drives expression in for each species of plant. There is a high degree of unpredictability about which substitutions or deletions would be tolerated.

Therefore, given the breadth of the claims; the lack of guidance and working examples; the unpredictability in the art; and the state-of-the-art as discussed above, undue experimentation would be required to make and use the claimed invention, and therefore, the invention is not enabled throughout the broad scope of the claims.

The Applicant argues that Donald demonstrated that a promoter fragment can be used regardless of its orientation and relative position as long as particular sequence elements like the G, I, or GT box are not destroyed by mutation, and that these boxes are only 12-14 base pairs and represent only a minor part of the rbcS-1 sequence (see paragraph bridging pages 17-18 of the response). This is not persuasive, because these data demonstrate the unpredictability. Motifs of only 12-

14 bases in length are essential for retaining the activity of the promoter. This is why internal deletions, substitutions, and insertions within a promoter are so unpredictable.

The Applicant argues that Kim teaches a symmetric structure consisting of a spacer regions surrounded by hexamers or palindromes that can be identified by pure sequence analysis, and Kim supports a proposition that mutations in these sequence elements do not necessarily abolish promoter activity (see second paragraph on page 18 of the response). This is not persuasive, because the extensive work that Kim et al did to determine the specific sequences required for the function of the nos promoter do not provide any information about the ptxA promoter of the instant SEQ ID NO:1. None of the information disclosed by Kim et al would aid one of skill in the art in providing direction or guidance about which domains, motifs, or subsequences of SEQ ID NO:1 are required for expression in substantially all vegetative plant tissues as recited in the instant claims.

The Applicant argues that Benfey teaches small fragments that one would not expect to retain the same expression pattern as the original promoter (see paragraph bridging pages 18-19 of the response). This is not persuasive because nucleic acids that have 98% identity, such as the nucleic acids encompassed by the instant claims, are not required to have any particular minimal length of contiguous bases of SEQ ID NO:1. The substitutions, deletions, and/or additions can occur anywhere within SEQ ID NO:1, and the instant specification has not provided any

guidance about what regions are sufficient or essential for expression in substantially all vegetative plant tissues as recited in the instant claims.

The Applicant argues that Benfey supports the proposition that it is routine to one skilled in the art to obtain a promoter fragment with the same expression pattern by a simple deletion analysis (see second paragraph on page 19 of the response). This is not persuasive, because the instant claims encompass nucleic acids with internal deletions, additions, and substitutions relative to SEQ ID NO:1, and this is different that fragments that have been truncated, but have not had internal changes. Furthermore, Benfey at et provide evidence that the tissue-specificity of the fragments is different in petunia plants compared to tobacco plants (see page 962), which provides support for the unpredictability of tissue-specificity from one plant species to another.

The Applicant argues that Benfey shows two putative CCAAT box sequences and a TGACG tandem repeat in the 35S promoter, and that this demonstrates that a person of skill in the art could identify which regions or elements of the promoter are essential for preserving function (see third paragraph on page 19 of the response). This is not persuasive, however, because the elements of the 35 S promoter do not provide any guidance that is relevant to the elements of the ptxA promoter of the instant invention. Therefore, the teachings of Benfey do not provide enablement for the nucleic acids of the instant claims.

The Applicant argues that identifying regions of a particular promoter sequence that are essential for the specific promoter activity is routine and not undue and there are numerous algorithms that can aid in this analysis and that the instant specification discloses these types of algorithms (see pages 20-22 of the response). This is not persuasive, however, because the claims are not directed to a method of identifying regions of the ptxA promoter that are essential for substantially vegetative expression, the claims are directed to nucleic acids that have this function. Furthermore, given the unpredictability in tissue-specificity of expression from one species of plant to another as discussed above, there is an added level of uncertainty with the ptxA promoter relative to other promoters.

The Applicant argues that the tissue specificity of the promoter is not unpredictable and species-dependent (see fourth paragraph on page 22 of the response). The Applicant argues that Bown's teaching that the endogenous ptxA gene being expressed strongly in pods but not in leaves or petals is not relevant because it is known in the art that the activity of an isolated promoter is not always identical with the expression level of a naturally occurring endogenous gene; and this can be due to the genomic environment of the locus or due to control mechanisms specific to the mRNAs (see paragraph bridging pages 22-23 of the response). This is not persuasive however, because the instant claims do not limit the genomic environment of the locus for the nucleic acid being claimed, nor do they limit the sequence of the mRNA transcribed. Therefore, any unpredictability due to

these factors remains an unpredictable factor for the instant claims. Furthermore, the prior art teaches that there can be variability between plant species with regard to tissue-specificity of a particular promoter, even when the identical construct is utilized (see Benfey, page 962, comparing expression in transgenic petunia relative to expression in transgenic tobacco, utilizing the identical constructs).

The Applicant further argues that the observation with the tomato homolog is directed to the endogenous tomato gene and that there is no significant sequence identity between the ptxA promoter and the tomato promoter (see second paragraph on page 23). This is persuasive, therefore, the Examiner withdraws the portion of the arguments that were directed toward the tomato homolog because they are not germane to the instant promoter of SEQ ID NO:1.

The Applicant argues that the Examiner has taken an inconsistent position by alleging that the tissue-specificity of the ptxA promoter is highly unpredictable, but also asserting that one would predict the ptxA promoter would drive expression in young tomato fruit (see third paragraph on page 23 of the response). The Examiner agrees and withdraws any arguments directed to tomato fruits.

The Applicant argues that an isolated ptxA promoter would not have a different expression pattern in any species other than Arabidopsis or Canola based on the expression of the endogenous gene (see paragraph bridging pages 23-24 of the response). This is not persuasive, however, because it is known in the art, as discussed in Benfey, that a particular promoter can have different expression

patterns in different plant species, and taken together with the strikingly different expression pattern of the endogenous gene in pea, there is a high degree of unpredictability about which plant species would have substantially vegetative tissue specific expression utilizing the instant SEQ ID NO:1, and this unpredictability is even more pronounced when one includes nucleic acids having 98% identity to SEQ ID NO:1 which can have internal deletions, substitutions, and additions relative to SEQ ID NO:1.

With regard to claim 13, the Applicant argues that it is well recognized in the art that yeast, algae, and fungi can be used to multiply or maintain an expression construct (see third paragraph on page 24 of the response). This is not persuasive, however, because the Examiner is not aware of any published accounts of people utilizing yeast, algae or fungi as host cells for maintaining a plant expression construct. It is well known in the art that plant expression constructs are usually maintained in E. Coli, and they are frequently maintained in Agrobacterium because Agrobacterium are utilized for plant transformation. It is not a common laboratory practice to utilize yeast, algae or fungi to maintain plant expression constructs, and the Examiner is not aware of any instance of such use.

Claim Rejections - 35 USC § 103

16. Claims 1, 3, 8-15, and 22-25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Henkes et al (US 2003/0140380, published on Jul. 24, 2003; and filed as App. No. 10/293,958 on Nov. 12, 2002, with priority to Nov. 9, 2001) as evidenced by Bown, D.P. (GenBank Accession X67427, published on Oct. 29, 1997; pp. 1-3) for the reasons of record stated in the previous Office Action mailed on Mar. 13, 2008. The Applicant's arguments in the response filed on June 30, 2008, were fully considered but were not found to be persuasive.

The claims are drawn to a construct comprising a promoter sequence that is a functional equivalent homolog having at least 98% identity to SEQ ID NO:1 or comprising a sequence from about base pair 300 to about base pair 583 of SEQ ID NO:1 and to vectors, organisms, plants, cell-cultures, parts, or propagation materials comprising said construct.

The instant claims are obvious over the prior art because there was some teaching, suggestion, or motivation in the knowledge generally available to one of ordinary skill in the art to combine the reference teachings, and there was a reasonable expectation of success in combining the teachings.

SCOPE AND CONTENT OF THE PRIOR ART – PRIMARY REFERENCE

Henkes et al teach a construct comprising a "super promoter", a "desired gene", and the NOS polyadenylation signal (see Figure 1). They teach a transgenic

plant comprising this construct; including monocots and dicots (see claims 9-12). They teach seeds which are "parts" of plants and are "propagation material" derived from the transgenic plants (see claims 15 and 16). They teach the use of a binary vector for transformation of plants (see paragraph 0098 on page 14). They teach the PtxA promoter from GenBank Accession # X67427 as a stress inducible promoter, and they suggest that it can be used in one of the preferred embodiments of their invention (see paragraph 0107 on page 16).

DIFFERENCES BETWEEN THE CLAIMED INVENTION AND THE TEACHINGS OF HENKES ET AL

Henkes et al do not teach the sequence of SEQ ID NO:1, nor do they teach any particular tissue specificity of expression.

SCOPE AND CONTENT OF THE PRIOR ART – SECONDARY REFERENCE

Bown teaches the ptxA promoter (see GenBank Accession X67427) which comprises a sequence that is 100% identical to the instant SEQ ID NO:1 (see sequence alignment).

LEVEL OF ORDINARY SKILL IN THE PERTINANT ART

The pertinent art is the field of molecular biology, and one of ordinary skill in this art would have earned a Ph.D. in molecular biology, biochemistry, plant biology, or some other related field; as evidenced by the skill level of Bown and Henkes, and the co-authors/co-inventors of Henkes. One of ordinary skill in this art would have been well-versed in techniques for heterologous expression of

recombinant proteins and would be familiar with the literature encompassing different inducible plant promoters and would appreciate the utility of stress-inducible expression of recombinant proteins.

FINDING OF OBVIOUSNESS

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to combine the teachings of Henkes et al and Bown. These teachings include each element recited in the instant claims, with the exception of the particular tissue-specificity recited. Because Henkes et al teach that it is a preferred embodiment to utilize a stress-inducible promoter and they specifically suggest the PtxA promoter taught by Bown (see paragraph 0107 on page 16), one of ordinary skill in the art would have been motivated to combine the teachings of Bown and Henkes to arrive at the instant invention. One would have had a reasonable expectation of success for expressing recombinant proteins in response to stress in plants transformed with the construct.

The property of expressing predominantly in leaves in Arabidopsis and canola is an intrinsic property of the ptxA promoter, and therefore, although Bown and Henkes do not teach this property, it would naturally flow from the combination of Henkes et al and Bown. A mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. See *In re Baxter Travenol Labs.*, 952 F.2d 388, 21 USPQ2d 1281 (Fed. Cir. 1991), where the court held that the fact that another advantage would flow naturally from following

the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.

For these reasons, the instant claims are obvious over the prior art.

The Applicant argues that Henkes does not teach, or even suggest that the desired gene could be a selection marker, a reporter gene, or a nucleic acid sequence which, when expressed, results in the production of an antisense RNA or double-stranded RNA, or increases quality of food and feed, produces chemicals, fine chemicals or pharmaceuticals, or confers resistance to herbicides or male sterility (see fourth paragraph on page 25 of the response). This is not persuasive, however, because it was well known in the art that "desired" genes could be selection markers, reporter genes, or confer resistance to herbicides or any of the other possibilities recited in the amended claim 1. None of these recited nucleic acid sequences are novel, and the Examiner takes official notice that these types of nucleic acids were well-known in the art and would be considered "desired" genes.

The Applicant argues that one would not have been motivated to combine a stress inducible promoter with any of the nucleic acid sequences recited in claim 1 (see last paragraph on page 25 of the response). This is not persuasive, however, because the use of reporter genes operably linked to any type of promoter were well known in the art, and one of ordinary skill would have been motivated to make such a construct to be able to track the activity of the promoter.

The Applicant argues that one would not have had a reasonable expectation of success that the ptxA promoter would drive the expression of any of those genes in a vegetative-tissue specific fashion (see paragraph bridging pages 25-26 of the response). This is not persuasive, however, because Henkes specifically suggests the ptxA promoter of GenBank Accession X67427, and this promoter comprises the instant SEQ ID NO:1 in its entirety with no mismatches. Therefore, the activity of expressing in vegetative tissues in Arabidopsis and Canola is an intrinsic property of this promoter, and even though it is not taught, it would necessarily be present in the construct suggested by Henkes.

17. Claims 1, 3, 8-15, and 22-25 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Arntzen et al (US Patent No. 6,395,964; issued on May 28, 2002) in view of Bown, D.P. (Thesis, Dept. of Biol. Sci., Univ. of Durham, Durham, UK (1992)), as evidenced by Bown, D.P. (GenBank Accession X67427, published on Oct. 29, 1997; pp. 1-3) for the reasons of record stated in the previous Office Action mailed on Mar. 13, 2008. The Applicant's arguments in the response filed on June 30, 2008, were fully considered but were not found to be persuasive.

The claims are drawn to a construct comprising a promoter sequence that is a functional equivalent homolog having at least 98% identity to SEQ ID NO:1 or comprising a sequence from about base pair 300 to about base pair 583 of SEQ ID

NO:1 and to vectors, organisms, plants, cell-cultures, parts, or propagation materials comprising said construct.

The instant claims are obvious over the prior art because there was some teaching, suggestion, or motivation in the knowledge generally available to one of ordinary skill in the art to combine the reference teachings, and there was a reasonable expectation of success in combining the teachings.

SCOPE AND CONTENT OF THE PRIOR ART – PRIMARY REFERENCE

Arntzen et al teach transgenic plants expressing oral antigens for use in oral immunization of animals (see entire document). They teach that the plant that expresses the antigen acts as both as an immunogen and an adjuvant, and that the transgenic plant material can be fed to animals (see abstract). They teach that the plants can be monocots; such as corn, rice, barley, wheat and rye; and dicots; such as sunflower, soybean, cotton, rapeseed, and tobacco (see second paragraph in column 7), and that the protein expressed by the transgenic construct should be expressed in edible transgenic plant tissues (see lines 45-50 in column 9); these edible tissues are "parts" derived from the transgenic plants. Arntzen et al teach vectors that comprise expression cassettes comprising promoters operably linked to coding sequences and further comprising polyadenylation signals which are additional functional elements (see Figure 1).

DIFFERENCES BETWEEN THE CLAIMED INVENTION AND THE TEACHINGS OF ARNTZEN ET AL

Arntzen et al do not teach the ptxA promoter, nor do they teach expression in vegetative tissues without expression in seeds, nor do they teach expression of GUS.

SCOPE AND CONTENT OF THE PRIOR ART – SECONDARY REFERENCE

Bown teaches the ptxA promoter (see pages 129-131 – note that ptxA is designated as pPP590) which is 100% identical to the instant SEQ ID NO:1 as evidenced by GenBank Accession X67427 (see sequence alignment). Bown conducted experiments to determine the expression patterns of the endogenous ptxA gene in *Pisum Sativum*, and he determined that it was expressed strongly in pods, but not in leaves, and only weakly in petals (see second paragraph on page 126; pPP590 is the clone of the ptxA gene). Pea pods are edible, and therefore, this suggests the use of the ptxA promoter to initiate transcription in an edible plant part.

LEVEL OF ORDINARY SKILL IN THE PERTINANT ART

The pertinent art is the field of molecular biology, and one of ordinary skill in this art would have earned a Ph.D. in molecular biology, biochemistry, plant biology, or some other related field; as evidenced by the skill level of Bown and Arntzen, and the co-authors/co-inventors of Arntzen. One of ordinary skill in this art would have been well-versed in techniques for heterologous expression of recombinant proteins and would be familiar with the literature encompassing different tissue-specific plant promoters and would appreciate the utility of tissue-specific expression of recombinant proteins.

FINDING OF OBVIOUSNESS

At the time the invention was made, it would have been obvious and within the scope of one of ordinary skill in the art to combine the teachings of Arntzen et al and Bown. These teachings include each element recited in the instant claims, with the exception of the particular tissue-specificity recited. Because Arntzen et al teach that it would be beneficial to express recombinant immunogens in edible plant parts, one of ordinary skill in the art would have been motivated to combine the teachings of Bown and Arntzen to arrive at the instant invention.

Bown teaches the ptxA promoter and teaches that the expression of ptxA in peas is predominantly in the seed pods which is the edible portion of the plant, therefore, one of ordinary skill in the art would have been motivated to utilize the promoter taught by Bown in the invention taught by Arntzen et al to arrive at the instant constructs, vectors, and host cells. One would have had a reasonable expectation of success for expressing recombinant proteins in seed pods of pea plants transformed with the construct.

The property of expressing predominantly in leaves in Arabidopsis and canola is an intrinsic property of the ptxA promoter, and therefore, although Bown does not teach this property, it would naturally flow from the combination of Arntzen et al and Bown. A mere recognition of latent properties in the prior art does not render nonobvious an otherwise known invention. See *In re Baxter Travenol Labs.*, 952 F.2d 388, 21 USPQ2d 1281 (Fed. Cir. 1991), where the court

held that the fact that another advantage would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious.

For these reasons, the instant claims are obvious over the prior art.

The Applicant argues that Bown teaches seed pod specific expression, but not other edible parts of plants such as leaves (see last paragraph on page 26 of the response). This is not persuasive, because as long as the expression is in an edible tissue (such as a pea seed pod) it satisfies the need of the invention taught by Arntzen et al, because it could be utilized to produce an edible vaccine.

The Applicant argues that the transgenic plants obtained from such combined teaching would not have an intrinsic property to express in the vegetative tissues such as leaves (see last paragraph on page 26 of the response). This is not persuasive, however, because the instant SEQ ID NO:1 has the property of expressing in the leaves of Arabidopsis and Canola, and therefore, a construct comprising SEQ ID NO:1 would have the intrinsic property of being capable of expressing in leaves of Arabidopsis or Canola if it were transformed into that particular plant species. The instant claims do not include any limitations on the species of plant, and therefore, being capable of directing expression in leaves of Arabidopsis or Canola is sufficient for satisfying the requirements recited in the instant claims.

The Applicant argues that the expression pattern of the tomato homolog does not remedy this deficiency (see first paragraph on page 27 of the response). This is persuasive, because the Examiner agrees that given the lack of sequence identity between the tomato homolog promoter and the ptxA promoter the expression pattern of the tomato homolog is not germane to the instant invention.

18. No claim is allowed.

19. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

20. Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHY K. WORLEY whose telephone number is (571)272-8784. The examiner is on a variable schedule but can normally be reached on M-F 10:00 - 4:00, with additional variable hours before 10:00 and after 4:00 with additional variable hours before 10:00 and after 4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on (571) 272-0975. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Cathy K. Worley/
Patent Examiner, Art Unit 1638